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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/563,440 | 01/05/2006 | Stephen Robert Wedge | 056291-5226 | 1233 |

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| EXAMINER | |
|---|---|
| SIMMONS, CHRIS E | |
| ART UNIT | PAPER NUMBER |
| 1612 | |
| MAIL DATE | DELIVERY MODE |
| 07/22/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/563,440 | WEDGE, STEPHEN ROBERT | |
| | Examiner | Art Unit | |
| | CHRIS E. SIMMONS | 1612 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *15 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,2 and 5-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 5-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 103*

Claims 1, 2, and 5-8 were rejected under 35 USC 103(a) as being unpatentable over US 2003/0055024 ('024) in view of WO 01/74360 ('360) and US 6,420,335 ('335).

**This rejection is maintained.**

Applicant disagrees with the rejection and states any such *prima facie* obviousness that might be said to arise from these references is overcome by the unexpected and significantly improved results achieved by the combination therapy as now claimed, as demonstrated at pages 16-19 of the specification, graphically illustrated in Figure 1, and discussed further below at pages 11-12.

The Examiner believes Applicant has examples with data showing unexpected results when a certain regimen of "concurrent" administration with AZD2171 and ZD6126 is used. In the examples, the mice were treated with AZD2171 (3 mg/kg/day orally) from day 0-day 14 and with ZD6126 (100 mg/kg/day i.p.) from day 0-day 2, where AZD2171 was dosed 2 hours prior to ZD6126 from day 0-day 2 and ZD6126 administration is not administered after day 2, wherein there is a 60% tumor size regression at day 14.

This, however, is not viewed as being reasonably commensurate in scope with the claims. Whether the unexpected results are the result of unexpectedly improved results or a property not taught by the prior art, the objective evidence of

nonobviousness must be commensurate in scope with the claims which the evidence is offered to support. MPEP 716.02(d). In this case, the claims are directed broadly to simultaneous administration of AZD2171 and ZD6126. Since the instant claims have been amended to limit them to "simultaneous" administration of AZD2171 and ZD6126, then of particular interest is the meaning of the term, "simultaneous". The term is not defined in the specification in such a way to make clear that the term is limited to concurrent administration of AZD2171 from day 0-day 14 with ZD6126 from day 0-day 2, where AZD2171 is dosed 2 hours prior to ZD6126 from day 0-day 2 and ZD6126 is not administered after day 2.

Claims 1, 2 and 5-8 were rejected under 35 USC 103(a) as being unpatentable over US 2003/0055024 ('024) in view of US WO 00/47212 (WO '212) and US 6,420,335 ('335).

**This rejection is maintained.**

Applicant argues that nowhere in WO '212 is the specific combination of AZD2171 and ZD6126 suggested. Moreover, nowhere in WO '212 does it state that use of any compound of the WO '212 invention with other treatments will produce "surprisingly beneficial effects". The Examiner does not find this persuasive because in the WO '212 discloses combination therapy comprising administering compounds of the invention and N-acetyleolchinol-O-phosphate, which is ZD6126. AZD2127 is a preferred compound in that reference. Accordingly, the specific combination of AZD2171 and ZD6126 is, indeed, suggested in the WO '212 document.

Additionally, the reference discloses "the present invention is based on the discovery of **compounds** that **surprisingly inhibit** the effects of VEGF, a property of value in the treatment of disease states associated with angiogenesis and/or increased vascular permeability such as **cancer**..." (WO '212: page 2, lines 15-17). Since the discovery encompasses other treatments, including other **compounds** such as ZD6126, the reference, indeed, does state **surprising beneficial effects** using compounds of the reference with other treatments. Expected beneficial results are evidence of obviousness of a claimed invention, just as unexpected results are evidence of unobviousness thereof. MPEP 716.02(c). It is submitted that the WO '212 reference discloses expected beneficial results when the 2 compounds are used in combination therapy.

As for the unexpected results, they have not overcome the prima facie case of obviousness previously made by the Examiner for reasons set forth above.

## ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Correspondence***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRIS E. SIMMONS whose telephone number is (571)272-9065. The examiner can normally be reached on Monday - Friday from 7:30 - 5:00 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Chris E Simmons/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612